

ND



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
 United States Patent and Trademark Office
 Address: COMMISSIONER FOR PATENTS
 P.O. Box 1450
 Alexandria, Virginia 22313-1450
 www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/934,970	08/21/2001	Jose L. Boyer	03678.0064.CPUS01	8356

27194 7590 05/05/2004

HOWREY SIMON ARNOLD & WHITE, LLP
 BOX 34
 301 RAVENSWOOD AVE.
 MENLO PARK, CA 94025

EXAMINER

LEWIS, PATRICK T

ART UNIT PAPER NUMBER

1623

DATE MAILED: 05/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/934,970	Applicant(s) BOYER ET AL.	
	Examiner Patrick T. Lewis	Art Unit 1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 02 February 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-25 is/are pending in the application.
4a) Of the above claim(s) 2 and 16-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 3-15 and 22-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>02252004</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II in Paper No. 6 dated July 3, 2003 is acknowledged.
2. Claims 2 and 16-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 6 dated July 3, 2003.

Applicant's Response dated February 2, 2004

3. In the Response filed February 2, 2004, claims 3-6, 8, and 13 were amended; claim 1 was canceled; and claims 22-25 were added.
4. Claims 2-25 are pending. Claims 2 and 16-21 are drawn to a nonelected invention. An action on the merits of claims 3-15 and 22-25 is contained herein below.
5. The objection to the Abstract is withdrawn in view of applicant's amendment filed February 2, 2004.
6. The provisional rejection of claims 1, 4, 5, and 13 under 35 U.S.C. 101 as claiming the same invention as that of claims 3, 5, 16, and 6 of copending Application No. 09/643,138 has been rendered moot in view of applicant's amendment filed February 2, 2004.
7. The provisional rejection of claims 3, 6-12, and 14-15 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4, 16,

Art Unit: 1623

26, 30-34, 7-15, and 11 of copending Application No. 09/643,138 has been rendered moot in view of the terminal disclaimer filed February 25, 2004.

8. The rejection of claim 1 under 35 U.S.C. 103(a) has been rendered moot in view of applicant's amendment filed February 2, 2004.

9. Applicant's arguments with respect to claims 3-15 under 35 U.S.C. 103(a) have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 22-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 22-23 recite limitations wherein the P2Y₁₂ receptor antagonist is not embraced by instantly claimed formula I, specifically the compounds not reading upon a dinucleotide such as 2', 3' phenylacetaldehyde acetal ADP and 2' or 3' phenylcarbamate UTP. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

Art Unit: 1623

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

15. Claims 3-15 and 22-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Zamecnik US 5,049,550 (Zamecnik); Yerxa et al. U.S. Patent 6,323,187 (Yerxa); Kim et al. *Journal of Biological Chemistry* (1994), Vol. 269, pages 6471-6477 (Kim); and Markland et al. U.S. Patent 5,814,609 (Markland).

Claims 3-15 and 22-25 are drawn to a method of preventing or treating diseases or conditions associated with platelet aggregation comprising administering to a subject

Art Unit: 1623

a pharmaceutical composition comprising a therapeutic effective amount of P2Y₁₂ receptor antagonist compound, wherein said amount is effective to bind P2Y₁₂ receptors on platelets and inhibit ADR-induced platelet aggregation. The P2Y₁₂ receptor antagonist is limited to a dinucleotide compound of Formula I. Dependent claims limit the conditions or diseases treated or prevented and modes of administration. Claims 8-12 limit the method by requiring the administration of a fibrinolytic agent.

Zamecnik teaches the use of diadenosine 5',5'''-p¹,p⁴-tetraphosphate (AP₄A), or an analogue thereof, as an antithrombotic agent (column 3, lines 4-59). The invention is based on the discovery that the administration of exogenous AP₄A, or an analogue thereof, to a mammal inhibits platelet aggregation, and, therefore, reduces the incidence of thrombosis. Zamecnik further suggests using AP₄A as a model to design similar or more efficacious agents (e.g. synthetic analogs).

Zamecnik differs from the instantly claimed invention in that Zamecnik does not explicitly teach analogs wherein at least one of the 2'- or 3'-positions is OR₁ or OR₂ as instantly claimed. Although Zamecnik teaches the use of the compounds and corresponding analogs for the inhibition of platelet aggregation, Zamecnik does not explicitly teach the dinucleotides as P2Y₁₂ receptor antagonists. Zamecnik does not teach the use of the dinucleotide in combination with a fibrinolytic agent.

Yerza teaches the tetraphosphate compounds of Formula I (column 3, lines 15-50). The compounds of Formula I also include pharmaceutically acceptable salts, esters, and amides thereof. The instantly claimed compounds of Formula I embrace the esters and amides of Yerza when instantly claimed Formula II defines R₁ or R₂. Yerza

Art Unit: 1623

also teaches that these compounds are therapeutic compounds that are selective agonists of the P2Y₂ and/or P2Y₄ purinergic receptor.

Kim teaches that agonists of P2Y purinergic receptors inhibit or modulate platelet aggregation (page 6471, column 1).

Markland teaches compositions for the prevention of thrombus formation comprising contortrostatin (CN) and at least one thrombolytic agent (column 12, lines 6-32). Suitable thrombolytic agents include anisoylated plasminogen streptokinase activator complex (APSAC); tissue-type plasminogen activator (tPA); urokinase-type plasminogen activator (uPA); and fibrolase, a snake venom fibrinolytic agent.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the 2'- or 3'-position of the dinucleotide compound of Zamecnik (from OH to OAc, for example) in order to find more efficacious antithrombotic agents. Indeed, Zamecnik suggests modifications of the compounds for just such a purpose. One of ordinary skill would have been motivated to modify 2'- or 3'-position to the corresponding ester or amide based on the teachings of Yerza and Kim. Yerza teaches compounds of similar structure that are agonists of the P2Y₂ and/or P2Y₄ purinergic receptor, and Kim teaches that agonists of P2Y purinergic receptors inhibit or modulate platelet aggregation. It would have also been obvious to a person of ordinary skill in the art at the time the invention was made to use the compounds of the invention in combination with a fibrinolytic agent to treat various diseases associated with platelet aggregation. The use of materials in combination, each of which is known to function for intended purpose (i.e. inhibition of platelet aggregation), is *prima facie* obvious.

Conclusion

16. Claims 2-25 are pending. Claims 2 and 16-21 are drawn to a nonelected invention. Claims 3-15 and 22-25 are rejected. No claims are allowed.

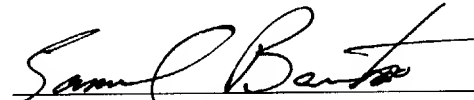
Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 571-272-0655. The examiner can normally be reached on M-F 10:00 am to 3:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patrick T. Lewis, PhD
Examiner
Art Unit 1623


Dr. Samuel Barts
Primary Patent Examiner
Technology Center 1600

ptl
April 30, 2004